

## Amendments to the Specification

Please replace paragraph [0052] with the following paragraph:

[0052] For example, octapeptides (P<sub>4</sub>-P'<sub>4</sub>) for MMP 2 and MMP 9 have been identified (see Table 1), which octapeptides simulate the cleavage sequence of the collagen chain and are cleaved with particular efficiency by MMP 2 and 9 (in what follows, amino acids are abbreviated in accordance with the international three-letter code):

Table 1:

### Peptide

P<sub>4</sub> P<sub>3</sub> P<sub>2</sub> P<sub>1</sub> P'<sub>1</sub> P'<sub>2</sub> P'<sub>3</sub> P'<sub>4</sub>

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Gly-Pro-Leu-Gly--Ile-Ala-Gly-Gln **[SEQ. ID No. 1]**

Gly-Pro-Gln-Gly--Ile-Trp-Gly-Gln **[SEQ. ID No. 2]**

(Netzel-Arnett et al., *Biochemistry* 32, 1993, 6427-6432)

[0054] Furthermore, in the case of cathepsin B, substrate-specific peptides are known with the sequence

-Gly-Phe-Leu-Gly- **SEQ. ID No. 3**

-Gly-Phe-Ala-Leu- **SEQ. ID No. 4**

-Ala-Leu-Ala-Leu- **SEQ. ID No. 5**

-Arg-Arg- or -Phe-Lys-

Werle, B., Ebert, E., Klein, W., and Spiess, E. (1995), *Biol. Chem. Hoppe-Seyler* 376, 157-164; Ulricht, B., Spiess, E., Schwartz-Albiez, R., and Ebert, W. (1995), *Biol. Chem. Hoppe-Seyler* 376, 404-414).

Please replace paragraph [0055] as follows:

**[0055]** The peptide sequence that contains intended peptide cleavage points relevant for the target enzyme can also be constructed such that the intended peptide cleavage point is repeated a plurality of times, for example by:

-Gly-Pro-Leu-Gly--Ile-Ala-Gly-Gln-Gly-Pro-Leu-Gly--Ile-Ala-Gly-Gln **SEQ ID No. 6**

or

-Phe-Lys-Phe-Lys-Phe-Lys-Phe-Lys-Phe-Lys-Phe-Lys- **SEQ. ID No. 7**

or a repetitive peptide sequence can be integrated that increases the distance between the thiol-binding group and the relevant intended peptide cleavage point, as for example by:

-(Gly)<sub>n</sub>-Phe-Lys-Phe-Lys- **SEQ ID No. 8**

with, preferably,  $n = 2$  to  $20$ , more preferably  $n \leq 12$ .

Please replace paragraph [0084] as follows:

**[0084]** Here the octapeptide

Gln-Gly-Ala-Ile-Gly-Leu-Pro-Gly **SEQ. ID No. 9**

derivatized with maleinimidoglycine 1 (Mr 848, prepared by solid-phase synthesis by Bachem AG, Switzerland) was reacted with doxorubicin according to the following method:

**[0087]** The peptide sequence Gln-Gly-Ala-Ile-Gly-Leu-Pro-Gly **SEQ. ID No. 9**

is recognized by the matrix metalloprotease MMP 9 and cleaved between isoleucine and glycine. This was shown by the following experiment: 200  $\mu$ L of a 100  $\mu$ M

solution of HSA-Cys<sup>34</sup>-2 was incubated for 30 minutes at 37 °C with trypsin/aprotinine-activated MMP 9 (2 mU, from Calbiochem, Germany). The liberation of DOXO-Gln-Gly-Ala-Ile due to cleavage with MMP 9 was confirmed by HPLC gel chromatography (Biosil 250 SEC column from Biorad, detection at  $\lambda$  = 495 nm) before incubation (t = 0, compare Fig. 2A) and after an incubation time of 30 minutes with activated MMP 9 (t = 30, compare Fig. 2B).

At the Examiner's request, Applicant is supplying a clear copy of the structure at the top of page 25 (attached at end of this paper).